Renewable and Sustainable Energy Reviews 16 (2012) 2102–2110

Contents lists available at SciVerse ScienceDirect

Renewable and Sustainable Energy Reviews

journal homepage: www.elsevier.com/locate/rser

Toxicological aspects of nanomaterials used in energy harvesting consumer electronics☆

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ARTICLE INFO

Article history:
Received 7 September 2011
Accepted 9 January 2012
Available online 18 February 2012

Keywords:
Photovoltaic cells
Fullerenes
Carbon nanotubes
Toxicology
Environmental impact

ABSTRACT

Sustainable energy harvesting, such as solar energy, depends increasingly on nanotechnology components. This article will look briefly at the principles of photovoltaic units and elucidate the toxicological aspects of its principal components, namely fullerenes and carbon nanotubes. Through this approach, we address the rebound effect related to health adverse and environmental aspects which is a key issue to be solved when innovating in energy harvesting. The understanding of sustainability in this context is that the technology provides lasting improvement by bringing environmental compatibility along with technological agility, providing major reductions in both material and energy resource use and avoid negative impacts on our environment and health. With the *rebound effect* we understand the unintended emergence of negative environmental impacts resulting from intentions of improving environmental issues.

Sustainable energy-harvesting, such as solar energy, depends increasingly on nanotechnology components. This article provides a brief overview of photovoltaic units and the toxicological aspects of their principal components, namely fullerenes and carbon nanotubes. It will then address the adverse, rebound effects on human health and the environment, the next key issue to be resolved within energy-harvesting innovation. Sustainability in this context, refers to the role of technology in providing lasting improvement through environmental compatibility combined with technological agility that enables major reductions in both material and energy resource use and minimizes negative impacts on health and the environment. The *rebound effect*, refers to the unintended emergence of negative environmental impacts as a result of remedial actions designed initially to improve the environment.

These will be discussed in context with the two major classes of nanomaterials in consumer electronics: *fullerenes* and *carbon nanotubes*, which carry a series of properties that make them classifiable as hazardous materials.

Contents

☆ This article is a condensed version of the manuscript "Fullerenes: A mini-review of a distinctive class of toxic nanoparticles" under writing for future submission.

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1364-0321/$ – see front matter
doi:10.1016/j.rser.2012.01.037

1. Nanomaterials in consumer electronics

Energy harvesting in mobile devices is foreseen to advance only in concert with miniaturization of electronics technologies [1]. In the move towards integrating more and more data, processing capacity is put into smaller and smaller components. Key to achieving this has been the use of various types of *nanomaterials*. Of particular relevance in electronics is the use of carbon nanotubes (CNTs) primarily because these materials have the following properties:

1. High structural and mechanical strength, making them well suited as structural components of electronics.
2. Very high electrical conductivity.
3. Very high thermal conductivity, thus a good cooling material for transfer of heat away from computer chips/processors.
4. Small diameter (<20 nm) facilitating further miniaturization of electronics components.

Fullerenes is another type of carbon nanomaterial which are increasingly being used in consumer electronics. For instance, C_{60} applies in certain types of the emerging technology of organic solar cells. However, there are concerns that CNTs and fullerenes released during their life cycle can have negative consequences on human health and the environment. This makes it important to assess the health and environmental aspects of CNTs applied in energy-harvesting devices.

2. Photovoltaic solar cells

In the organic photovoltaic solar cells, energy transfer occurs through the use of nanomaterials. In these cells, nanomaterials such as fullerenes and CNTs are principal components for achieving ultra-fast charge transfer, with a quantum efficiency approaching unity [2,3]. The nanomaterials are integrated in a conjugated manner, allowing them to reach femto-second charge transfers from light-impulses, thereby making the solar cells highly efficient in generating electricity [2]. The opto-electrical device is the key component of photo-voltaic cells that has a large surface area, is flexible, durable and light-weighted compared to regular microelectronics [4]. As in the case of chemistry type (wet or dry), the solubilization of the electron-transferring components and polymers remains, to date, the most applied technology for photovoltaic cells. The electron acceptors used in these nano-circuits must therefore have a significant solubility, and simultaneously be connected to the bulk material, to keep the interpenetrating networks phase-separated. The phase-separation (wet electron-transferring material to dry bulk material) is the key latency for these circuits, which bring naturally more resistance in conductivity. In these classical photovoltaic units, the improvements rely on reducing resistance and increasing photonic absorption, methods which are increasingly being solved through the use of nanoscale manipulation and architectures. Such an example is most recently published by Tada et al. [5], where the organic compounds poly(3-hexylthiophene) (P3HT) and [6,6]-phenyl-C61-butyric acid methyl ester (PCBM) are used as semi-conductors in nano-films which exert the principal electron transfer. These organic compounds prove particularly efficient given their optimal HOMO–LUMO electron gap, which delineates the most important aspect for defining the electron-transferring efficiency in an opto-voltaic unit. The HOMO-LUMO gap, depicts the energy gap between the lowest unoccupied molecular orbital of the electron accepting compound, and the highest occupied molecular orbital of the electron of the electron donating compound, in the charge transfer chain. Such gaps are therefore easily modulated, by changing the compounds. However, the wet processes have several disadvantages, and are extremely difficult to fabricate and to analyze through conventional techniques [5]. Secondary, wet-processes may lead to the formation of residual organic vapors which may affect both the efficiency and durability of the photovoltaic cells. Additionally to fullerene components, many of the photo-voltaic units have fluoro-alkylated side-chains in the conjugated networks, which act as the "spine" in the electron transferring nano-conjugates. TiO_2 coatings are also used, a material which is currently regarded as toxic.

The current wet-processes therefore contain a series of chemicals and materials which need toxicological profiling and procedures of classification. Hence the toxicological properties of buckyballs and carbon nanotubes, which may be unknown to many material scientists, are presented here in this article.

This can for that reason, impel the current nanomaterial investigators to look for alternatives which reflect a better compatibility with the environment.

3. Buckyballs

Fullerenes (buckyballs, C_{60}) are a group of carbon nanomaterials, formed as spheres, which range from C_{20} to C_{720} (and larger) and are composed of 20–30, 720 and more carbon atoms, arranged as empty closed cage structures, and made up of multiple 5-member and 6-member rings depending on the size [6] (Fig. 1). Their use is primarily allocated to medical and bio-nanotechnology applications, given that they exhibit a wide range of biological activities [7]. Areas of applications are: transport of drugs through dense tissues such as tumor-tissues, applications in DNA photo-cleavage, and gene delivery [8]. Fullerenes are also applied in environmental remediation, where they are used, for instance, in pathogen

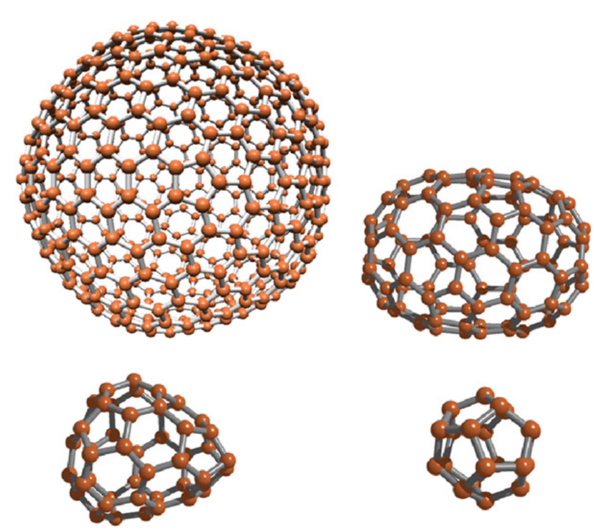

Fig. 1. Various fullerenes in different shapes and sizes. From top left to bottom right: a C_{500} fullerene; a C_{96} fullerene; a C_{46} fullerene; a C_{20} fullerene. The 6-carbon rings are seen adjacent to the 5-carbon ring in a well-organized manner, and the smaller they become, the more 5-members rings they gain, increasing also their reactivity.

decontamination [9]. Fullerenes are also used in energy systems such as in organic solar cells [10,11] where their function relies on their unique and highly versatile electronic properties. An example of such properties is the case where upon illumination as part of a solar cell, fullerenes free electrons which are generated at the junction with the resin they are bound with [12]. In other words, fullerenes give completely novel aspects to these various applications in the industry. Fullerenes are also, as mentioned, used in drug delivery given their transmembrane passing-ability. An example of their application in medicine was demonstrated by Jiao et al. on the ability of fullerenes to down-regulate the oxidative stress in the lung tissue of tumor-bearing mice [13], yet other examples delineate of selective drug-delivery, for example, as in the case of diabetes [14]. In medical screening, fullerenes are also applied, for example, where single metal atoms are encapsulated in a buckyball to serve as absorbers in bio-markers [15]. Furthermore, fullerenes have also been applied with bio-molecules, in order to promote specific functions, such as catalysis of hydrogen peroxide [16].

3.1. Health-adverse aspects of fullerenes

Fullerenes have been widely studied for their negative health impacts and have shown to be interfering with several mechanisms in the body of animals and humans. These effects vary according to the format of the fullerenes, and their chemical modified state. However modified, the principal toxicological property of fullerenes is carried by their apolar character which is compatible with merging with biological membranes in organisms [17,18].

In a study by Nakagawa et al. [17] hydroxylated fullerenes (fullerenoles) were tested on rat hepatocytes. The fullerenes showed strong detrimental effects and induced cell death within 3 h in the rat liver cells. Furthermore, several crucial cellular factors, such as ATP and thiol levels were depleted by the fullerenes. The fullerenes caused also substantial damage on the mitochondrial membrane, particularly the highly hydroxylated fullerenes types.

These results showed that the semi-hydroxylation of fullerenes increases solubility and thereby the ability of the fullerenes to dissolve membranes, acting on both the cellular and intracellular membranes. Nagakawa et al. [17] also found that of the several membranes present in hepatocytes, the mitochondrial membrane was the membrane that was most negatively affected. This leads directly to dysfunction of the energy generating units and dissolution of the organelle membrane [17]. Thus, in this study we ask an important question: *Will the modification from pristine C_{60} to hydroxylated C_{60} or other chemical modifications solubilizing fullerenes, increase the hydrophilic property such that it can act as a transporter of water molecules through the lipid bilayer, such as in the case of hepatocytes?*

This mechanism presents a unique and perhaps novel aspect within toxicity, where innocuous molecules such as water are transported by the toxic agent into domains within the cell where they become detrimental and act as co-contaminants. This mechanism may include many other co-contaminants, however the co-binding of other contaminants may also increase the variation of fullerene intoxication types, and give rise to the emergence of more mechanisms of toxicity by fullerenes.

An additional observation on fullerenes and their solubilization is seen in context with their increasing resemblance to biological factors (which are amphiphilic and charged). The modifications of fullerenes may lead to a resemblance to cellular components, particularly proteins. This is further strengthened by their spherical structure, amphiphilic nature and stable conformation. This may therefore make it is easier for fullerenes to pass by the body's defense system, "unhindered", making fullerenes harder to be identified and degraded, rather than easier to be identified as in the case of non-hydroxylated fullerenes. Such a mechanism of increased toxicity through increasing bioavailability via "bio-resemblance" was observed by Drug et al. [19], where toxins were more efficiently transported throughout the lungs via their compatibility with the tissue. The question on fullerenes and increasing bio-availability upon modification is therefore a critical point which needs to be investigated, whenever these nanomaterials are implemented in consumer electronics, as for instance in energy generating units.

3.2. Aquatic studies on fullerenes

Fullerenes have also shown to cause eco-toxicity. In a recent study, the effects of fullerenes (C_{60}) on zebra fish's ability to uptake hormones from aquatic environments were assessed [20]. This study emphasized the presence of nanoparticles in the environment with particular focus on the negative aspects of fullerenes as bio-interfering particles. The study also focuses on the difficulty in determining the concentrations of these very nano-particles in ecological studies, because of their behavior in water. Fullerenes are able to form aggregates, ranging to multiple nanometers in diameter. These aggregates were formed accordingly with the reaction of fullerenes to water and to each other, where water repelled the pristine fullerenes and forced them to form aggregates [20]. These nano-aggregates were then shown to affect the uptake of estradiol derivates, and induce hormonal changes in the Zebra fish [20].

Also, fullerenes are particularly susceptible to other chemical compounds, which delineates the ability of fullerenes to bind metals, particularly heavy-metals and various organic compounds. In this context, it is hypothetically sound to suggest that fullerenes may act as transporters and deprive soil chemistry for important nutrients and chemical compounds that are central for local organism's development, and their part in the ecological metabolic chain. This hypothesis the study by Park et al. [20], who reported that C_{60} fullerenes aggregate in nano-particles of diameter of ∼200 nm and bind strongly to organic matter of which much may be nutritional organic matter for small species – such as plankton in aquatic systems.

The interference with hormonal uptakes in aquatic system showed serious toxicological aspects [20], and illustrates how a man-made agent may be sufficient to pose a threat to the reproduction cycle of an entire aquatic species. The results showed also that the uptake of C_{60} in the intestinal tract of the Zebra fish was quite efficient, reaching almost 100% [20].

Similar observations of aggregates have been made in aquatic studies by Jovanović et al. [21] and Kim et al. who used different carriers of C_{60} in their study on fish embryos [22]. Their results showed how aggregates of C_{60} in combination with aromatic compounds (experimentally used and tested as carriers) affected embryonic development which classified fullerenes as teratotoxic [22,23] and how fullerenes inhibited neutrophil function [21]. These results showed that the most commonly occurring consequence of the intoxication of C_{60} suspended in toluene in fish embryo was mortality, the second was deformity [22]. C_{60} was also found in this study to be able to carry/be carried by DMSO, a strongly polar compound, through the embryonic cells. This caused a much higher effect on malformation and delayed development of the fish embryos. In combination with water only, C_{60} induced mortality in 28% of the embryos [22]. The explanation for these effects was demonstrated by the ability of pristine C_{60} (without hydroxyl groups) to penetrate the cell membrane [24], and its ability to bind co-contaminants. In a co-contaminated situation, as for instance in an oil/gas leakage, the fullerenes may act to increase toxicity, with different carrier molecules [22]. Therefore, the availability of C_{60} suspensions in aquatic environments may affect reproduction, and create significant problems for marine species that rely on smaller organisms which attempt to metabolize or are intoxicated by C_{60} aggregates.

Fullerenes have also been found to affect monocellular organisms such as bacteria [25,26]. Entire ecosystems depend on bacteria and monocellular organisms such as diatoms in the circulation and transformation of gases and biochemical compounds, from the atmosphere to the aqueous phase, and in soil. The high presence of fullerenes in modern society may, therefore promote a significant need for ecotoxicological assessments in addition to the adverse impacts on human health. This delineates the importance of studying fullerenes within aqueous environments in environmental sciences for the specific purpose of mapping trans-ecosystem consequences to document eventual long-termed effects between land, ocean and air ecology, if such products should be as well incorporated as plastics have been in the last decades [27].

3.3. Mutagenicity of fullerenes

Fullerenes have also been shown to induce mutagenicity. A group of scientists showed that C_{60} fullerenes induced genotoxic effects on a human lymphocyte cell model, with strong correlation with the concentration of fullerenes [28]. The results also showed that quite low concentrations of fullerene were required to induce negative effects on the cell model, reaching as low concentrations as 2.2 μg/L. The results may also be contemplated with the particle-to-concentration principle by Oberdörster et al. [29], which states that the effect of a low concentration may still be high, given the high number of molecules. Additionally, the size distribution of fullerene aggregates was observed in the study [28] to be highly variant, where single-molecule and multi-molecule aggregates of C_{60} dispersed in the ethanol and aqueous solutions were found [28]. The behavior of fullerene C_{60} in solution is therefore the foundation for generating nano-aggregates of these dimensions, which in turn are responsible for the observed effects [17,22,23,28]. The results from the study [28] also showed that nC_{60} (aggregates) produce oxygen radicals as earlier found [29–31] which induces leakage from the cytoplasmic membranes. Also, oxidated C_{60} (carboxy-C_{60}) has been shown to cut DNA sequences at the guanine sites, possibly through photo-activation [32,33]. The mechanisms of DNA damage appear dependent on C_{60} either interacting with reactive oxygen species in the nucleus promoting catalytic activities cutting the DNA, or the oxidative effects on the DNA through its oxidated carbon atoms.

Several other aspects of C_{60} have also been identified. They pass through the cell membrane within a period of 15–30 min, and the reactions occurring within the cell swiftly take place after intoxication [34]. Such reactions have been discussed here, but a surprising toxicological aspect of fullerenes is their ability in avoiding lysosomes [34], which are the cells natural defense against foreign matter. Such a feature makes fullerenes "intelligent" toxicological particles, thereby showing additional aspects of their unusual toxicological behavior. Indeed, such an action induces more inflammatory responses, and given that the lysosomes are unable to engulf the C_{60} and be secreted, the secondary reaction becomes by necessity the free expression of ROS within the cytoplasm. Freeing ROS is a risk which the cell takes, given ROS species attack the cells own components. Based on the reviewed reactions of fullerenes in fish and on genotoxicity [28], a case of lysosome-avoidance may therefore promote substantial problems for the inflammatory cells [28,32,33].

These reported findings are crucial in establishing guidelines for developing and discarding consumer electronics as an emerging application in society. In order to produce better and more sustainable consumer electronics, fullerenes, which are increasingly being applied in this field, should be selected accordingly with their mentioned properties and be properly listed in components for product labeling and safety issues.

4. Carbon nanotubes (CNT)

Carbon nanotubes (CNT) are nano-structures which are entirely composed of carbon (in their original unmodified state) and can have diameters of 1–100 nm and lengths up to several micrometers [35–40]. CNTs have unique physicochemical properties including semiconducting and metallic electrical behavior, high mechanical strength and unique chemical and surface properties. Potential applications include mechanical actuators, microelectronic devices, catalysis, sensors, high-strength composites, and adsorbents [41–48]. In these fields, CNTs have been implemented as damage-sensors, where their electrical properties are used to detect cracks and physical stress in materials [49]. Such applications of damage sensing with CNTs can be applied in automotive vehicles and aerospace constructions for instance, where the conductivity and strength of CNTs is the main advantage. Other recent applications are the use of CNTs in lithium batteries as storage structures, where the CNTs are combined with graphene sheets in order to provide solid energy-storing nano-ensembles [50]. CNTs are also widely used in bio-nanotechnology nano-architectures, such as in assembly with DNA [51], and for bio-sensing purposes to detect ultra-low levels of bio-molecules in medical and laboratory samples [52]. Ultimately, CNTs are extensively used for novel applications in biomedicine for delivery of drugs [53].

CNTs have also been recently incorporated in computer components, for the synthesis of nano-processors [54], where the electronic properties of CNTs prove their advantage in nano-electric circuits. Their electronic properties also make CNTs crucial for construction of 1-dimensional structures, where peculiar electronic phenomena occur, such as spin-charge separation making the nano-electric structure superconducting [55]. In these structures, "electron-liquids" are constructed in combination with CNTs, making it possible to gain super conductivity as "liquid nano-wires" [55].

4.1. Types of carbon nanotubes

CNTs are subdivided into two main classes, single walled nanotubes (SWCNT) and multi-walled nanotubes (MWCNT). SWCNTs consist of a single sheet of graphene which is rolled into cylinders with diameter of 1 nm and length of up to several millimeters [35–38]. Multi-walled nanotubes (MWCNT) consist of an array of such cylinders formed concentrically and separated by approximately 0.35 nm. MWCNTs can have diameters from 2 to 100 nm and lengths of several micrometers [56]. Double-walled carbon nanotubes (DWCNT) are also representing an own type of nanotubes, which is used for similar purposes as mentioned above [57]. These are easier to work with than multi-walled carbon nanotubes given their double layer of rolled graphene sheets, and may be used for similar purposes as single-walled tubes, but with a stronger physical durability. Fig. 2 illustrates these types of CNTs.

4.2. Environmental aspects of carbon nanotubes

CNTs are under investigation from various groups given the concerns that are arising in context with their implementation in society. The primary issue is their contribution to the complex landscape of nanoparticles in the environment, in water, soil and air, where they add and potentially multiply the adverse aspects to human health and to the environment.

Recent reports on environmental pollution show that the deposition of nanoparticles reaches distant locations from their origin, as far as the Arctic and remote regions of the Pacific Ocean, inducing significant problems for organisms and animals in these otherwise un-touched habitats [58]. The majority of these particles are derived from plastics and exhaust emissions, however if

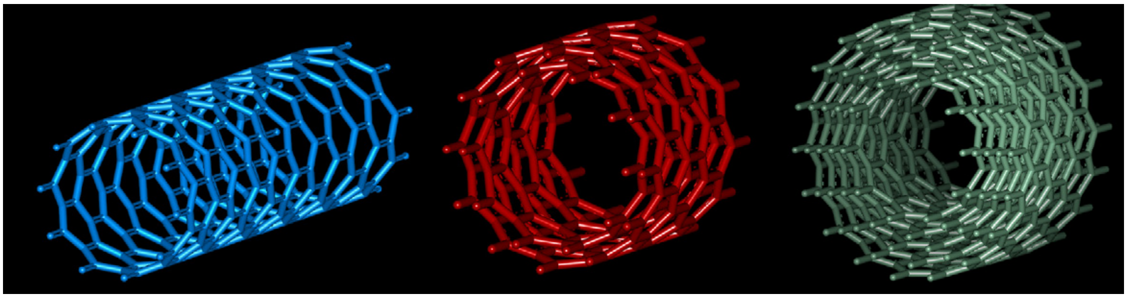

Fig. 2. An illustration of the three main classes of pristine carbon nanotubes: (left) single walled CNT, (middle) double-walled CNT, and (right) multi-walled CNT.

substantially produced, carbon nanotubes may quickly contribute to this critical situation, assimilating to the fate of plastics, where their deriving nanoparticles accumulate in the environment and become a part of the nutritional and reproductive environment of humans and animals [27,59,60].

In this context, carbon nanotubes are the target-group of concern for this study, because they represent a group of solid and ultra-stable nanoparticles with strong adsorptive properties, binding various molecules and biomolecules efficiently, potentially interfering with living organisms [61]. Additionally to the pristine carbon nanotubes, their chemically modified forms lead to an increment in the chemical variation of compounds released in the environment, requiring novel recycling policies that need to be updated with the chemical and nanotoxicological properties of modified and unmodified carbon nanoproducts. Also, toxicological assessments and protocols may need to be refined in accordance with the macromolecular properties of carbon nanotubes (e.g. interaction with DNA) and their nanoparticle character such as dimensions, aggregates, colloids and dispersions which shall be discussed here.

The secondary concern regarding carbon nanotubes evolves around their biopersistant character which has, in several occasions, related them to asbestos products [62,63]. In response, life-cycle studies on carbon nanoproducts and on their toxicological properties are increasingly being sought after, and European legislative organs are increasing focus on carbon nanoproducts for environmental studies and new regulations [64,65]. The current knowledge on carbon nanotubes in the environment is hereby stated to be scarce to the extent it is required for a full environmental policy for carbon nanoproducts. Their contribution to the environment and health is concluded in consensus, including that their contaminating, co-contaminating and bio-resistant properties are fully assessed and agreed on a multi-national level.

The exact knowledge of the concentration of carbon nanotubes in the environment is not known. In 2009 it was modeled that the amount of CNTs in the environment was quite low, encompassing concentrations of 0.003–0.02 ng/L [66]. The increase of the amount of carbon nanotubes in circulation in the environment is also unknown, but depends ultimately on the pace of their implementation in consumer products and society [66–68]. The initial guess of this pace was per 2008 based on an estimated yearly production of carbon nanotubes of 350 tons, of incorporated in consumer electronics and 50% in plastic products [68]. Out of these figures, the fate of CNTs which are not recycled (~45%) is presumed to be directed to incineration plants [68], where partial and full incineration of CNTs take place, depositing CNTs in the air and soil as carbon black and partially incinerated (fragmented, oxidized) carbon nanotubes.

Furthermore, based on guesses [68], the yearly deposition of carbon nanotubes in the environment is more than 150 tons per year, and increasing [68,69]. From this point, the ecotoxicological aspect plays a vital role for determining and setting a threshold for allowed concentrations of CNTs in the environment. However, this is still under investigation given that there are not enough studies to determine concentration limits for soil and water sources [68] and most studies are conducted in laboratories, based on theoretical assumptions on concentrations ranges.

4.3. Aquatic toxicology studies on carbon nanotubes

There is a substantial need for several studies on the effects of CNTs on various life forms, including bacteria, algae, fish, animals and humans. Some of the studies on CNTs have evolved around the currently low availability of CNTs in the environment and some show low or no effects on aquatic species, and decreased toxicity upon chemical modification [70,72]. It is however stated that our understanding of these nanoparticles is still too poor and current risk assessments are too few to evaluate the risk to organisms [68,72]. Ultimately, the unique properties of CNTs make them more difficult to be assessed given their various chemical properties, with unique macromolecular qualities combined with their nanoparticle qualities, differentiating them from ordinary polluting particles [72].

Carbon nanotubes and particles are showing various toxicological effects on organisms. In a study by Smith et al. [73] SWCNTs were found to harm rainbow trout, inducing organ pathology and affecting their respiratory function. The rainbow trout experienced increased ventilation rates after daily exposures to SWCNTs, the carbon nanotubes particularly affected the gills where they associated with mucous proteins. Interestingly, the SWCNTs also induced aggressive behavior in the fish, leading to increased fighting and dissolving the schooling behavior [73]. Increased mortality was observed towards the end of the experiment. Both mortality and aggression correlated with the concentration of carbon nanotubes. The aggressive behavior seemed to correlate with brain-inflammation induced by the SWCNTs in the fish with signs of aneurism and blood-vessel swelling, particularly in the anterior parts of the brain [73]. Affecting also ionic balances, an increase in K^+/Na^+ ATPase activity was observed in the fish exposed to SWCNTs, followed by signs of oxidative stress. In conclusion, the study by Smith et al. showed the potential of SWCNTs in bringing harm to schools of fish, their behavior and their health and in inducing health-adverse effects and mortality.

Separately, in a cell-study on rainbow trout macrophages the activation of interleukins was demonstrated, with however no lethal effects of SWCNTs on the various cell types tested [74]. The effects on the organism itself [73] are therefore quite different from the effect on cells alone [74]. This may be explained through the nanoparticle character of carbon nanotubes, which yields the complications on the whole organism through mechanical stress on gills and more exposed organs [73] rather than particularly potent molecular effects at the cellular level [74]. Such mechanical effects were observed on Zebra fish, where SWCNTs delayed hatching and attached to the pores allowing oxygen in the embryo [75], again

showing a mechanical intromission of CNTs as a nanoparticle. Interestingly, in this same study, DWCNT did not delay hatching to that extent as SWCNTs [75], something that may be explained either by their differing particle-diameter, or difference in electronic properties (which shall be endeavored here). However, in a separate study, DWCNTs showed to be highly toxic to three marine species, the diatom *Thalassiosira pseudonana*, copepod *Tigriopus japonicus* and medaka *Oryzias melastigma* [76]. The results showed that the preparation of the CNTs, either through sonication or stirring determined the toxicity of the nanotubes [76], something that may explain the toxicity studies showing low or no effect of CNTs [70,71]. Sonicated carbon nanotubes give smaller particle sizes and stronger toxicological effects in water [76]. Similar studies and approaches should be explored for aerosolic inhalation.

Studies on cells and organisms should be viewed as different perspectives of carbon nanotubes, where effects on cells should not be used to clear nanotubes as non-toxic, given that the very nanotubes tested for molecular interactions may induce lethal mechanical complications instead at the physiological level [73], depending on organism, and organ type [73,75]. Also, these very findings must be debated against the presence of natural occurring nanoparticles and nanotubes [77] for a gradual contemplation of the environmental effects of carbon nanotubes on organisms.

MWCNTs have also been found to induce negative effects on organisms. MWCNTs were found to induce vesicle development in the Zebra fish larvae, which leads to lower survival rates [78]. Carbon nanotubes have also recently found to be able to cross membranes and alter the mitochondrial gene expression, ribosomal function, induce inflammatory response and affect cell cycle [79].

Because of these findings, the importance of evaluating carbon nanoproducts, particularly carbon nanotubes in context with ecological settings is important. This was also stated in a recent symposium in Japan by Japanese scientists with particular concern on carbon nanotubes. Tsuda highlighted the lack of risk assessment projects in order to emphasize the need for better risk communication and risk management [80]. So far, only a limited amount of data has been gathered for carbon nanotubes, and thereby authorities and legislative organs do not have data to establish a solid foundation for risk management of carbon nanomaterials [80].

In the US, Japan and EU, a total of zero studies have been done on chronic toxicity (dermatological) tests on carbon nanotubes pr 2010 [80]. Because of this urgency, the need to estimate the concentration of nanoparticles occurring in the environment, and their various chemical forms including chemical fate is paramount.

This is particularly important because the amount of nanoparticles in the environment is growing at an unknown rate and is still unknown [80–83]. The reason for this is based on several factors: (1) there is an unknown amount of *naturally* occurring nanoparticles in the environment and their contribution to the effects by the unknown amount of *engineered* nanoparticles from the industry is not discovered, (2) the life-cycle and chemical fate of engineered nanoproducts is not mapped and (3) the effects of engineered nanoproducts on animals and humans is still largely unknown and debated.

4.4. Biocompatibility of carbon nanotubes and bioavailability – potential consequences for public health

Because of their peculiar nature, the toxicological aspects of carbon nanotubes can encompass a wide range of pathological mechanisms, and complicate the pathophysiological assessment for population diseases, if substantially present in circulation in the society. This is described through their route of exposure being situated in the lungs, GI tract and orifices by their ability to pass the blood barrier and be able to be located to neural and vital parts of the body such as the brain [83–86]. CNTs assimilate also unusually well with bodily tissues [86], and their deposition in the body and half life is poorly mapped.

The general biocompatibility of CNTs with the body's muscular filaments [86] may also be an important factor in evaluating how the presence of CNTs at substantial amounts in circulation in society may assimilate the mechanism of neurological syndromes that evolve around the aggregation of waste/toxic products in the nervous tissue, such as prion-diseases [87]. Prion-diseases are primarily caused by the terminal localization of biological/biochemical aggregates in the nervous tissue and brain [87] and are known to be difficult/unmanageable to cure. For this reason, carbon nanotubes need also to be evaluated for long-termed exposure studies at various concentrations so their complete biochemical fate in the body is documented using more realistic models accounting for such worse-case scenarios.

Till now, most of the studies available document the short-term effects of CNTs on animal models and cell models, which give only a partial picture of the eco-toxicological character of CNTs as described above, and their unknown aspect in context with public health, legislations and safety. For this reason, it is eminent that the studies of carbon nanotubes evolve around futuristic applications as contained in a precautionary principle and do not follow after long-termed cases of intoxication in the industry and society.

4.5. Aerosol toxicology studies of carbon nanotubes

CNTs present a series of complications as aerosol particles as well. The primary concern of CNTs is their interaction with the pulmonary system, through aspiration as aerosol particles [84–88]. The effect of carbon nanotubes on the lungs is three-fold: (i) direct damage to epithelial cells, (ii) encapsulation of carbon nanotubes into agglomerates and formation of granulomas, (iii) the inflammatory reaction to CNTs are molecular ensembles resulting in interstitial fibrosis and inflammation [89–92]. The inflammatory response to CNTs is propagated by polynuclear neutrophils subsequently followed by macrophages which induce rapid expression of pro-inflammatory factors [89]. These reactions lead to fibrosis, a type of inflammation of the lung fiber which can further develop into pulmonary complications causing lesions in the lung tissue [92]. The fibrosis which has been observed as a consequence of inhalation of CNTs in mice models, resembles alveolar damage and alternation, where a thickening of the alveolar walls was observed including lesion-development [90,92]. The sizes of nano-particles used in experiments also determine the test outcomes results on mice, something that may further complicate the assessment of CNTs for working and habitat environmental studies [74,93,94] and require more guidelines with regards to handling CNTs for experimental procedures [94].

The fibriotic effect of CNTs has also been compared to other known particles that induce respiratory problems. The comparison was made to black carbon, the main component in carbon mines that was disputed as a toxicological disaster in the early industrial age, and silica oxide particles, a known group of particles that induce the lung problem called silicosis. The comparison showed that CNTs induce a stronger fibriotic effect than both silicon oxide and carbon black [88,90]. This alarming strength of SWCNT to induce pulmonary complications was furthermore shown to reduce the ability of the lungs to clear bacterial infections as well [91], a condition that may lead to pneumonia and lung diseases.

SWCNTs ability to induce cellular changes and trigger apoptotic responses was also mapped where the generation of reactive oxidative species (ROS) were documented after that CNTs induced cytotoxicity in cells [90,91]. The generation of ROS also leads to systemic immune responses, as proved on animals in two other studies using MWCNTs [95,96] in addition to local reactions such as the

expression of various immunoglobulins, which varied according with the size and type of nanotube [95].

The knowledge on the presence of different immunological profiles to different types of nanotubes raises the notion that the problems connected to carbon nanoparticles may be more complex and far reaching than other contaminating particles. The macromolecular architectures of nanotubes, the potential rise in various sub-groups of contaminants (defined by different forms of the debris of fractionated and partly oxidized nanotubes in the environment) and alternative conformations may also lead to the observed variation of immunological expressions. Therefore, the nano-architectures separates nanotubes from other "conventional" toxic molecules compounds, something that gives CNTs the conventionally recognized *nano-toxicological* character [88–92]. The nano-toxicological character promoting alternative immunological profiles of expression can be said to give CNTs a *nano-immunological* response-mechanism as well, where different reactions are expected for different sizes and shapes of CNTs [95,96]. This notion has not been postulated earlier, but rather emerging within a reviewed profile of results [88–96]. As a crux to the immunological studies, nanotubes present a unique group of particles that require particular attention from toxicologists and public health legislators. Current toxicity studies are not sufficient to inform specific legislations and regulations on carbon nanotubes according to German regulatory scientists [97]. For this reason, CNTs demand more attention than previously given, because of the ubiquitous nature [98], and because of the nano-immunological phenomenon as deduced here. The effects of CNTs are potentially stronger than previously thought, this was shown in a recent study [99], which delineates why carbon nanotubes must be categorized as an own class of toxicological entities and defined into safety hazard classes before incorporation in the society.

In the referred study [99] the inflammatory potential of SWCTNs in the lungs has also been studied recently in mice C57BL/6 subjected to aspiration of SWCNTs on prolonged periods of time. The SWCNTs showed to be more inflammatory than asbestos and induced a greater abundance of inflammatory proteins than asbestos and carbon black. The reaction of SWCNTs in the pulmonary system was furthermore mapped to be 4–5 times stronger than the reaction to asbestos [99]. In context with the nano-immunological nature of CNTs, the reactions to asbestos in mice was defined by 231 proteins, to carbon black 184 proteins, while for SWCNTs a total of 376 proteins [99]. This delineates the multitude of reactions that are triggered by CNTs, which include leukocyte activation, apoptosis, fibrosis angiogenesis and other cellular and immunological reactions [99], which show a much more broader immunological complexity than strongly toxic particles as asbestos and carbon black. This feature and its importance were also noted by the authors [99], however not discussed in context with the nano-immunological phenomenon as postulated in this review. This study [99] sheds light on the deep complications that SWCNTs cause in the pulmonary system, and being 4–5 times more reactive than asbestos when inhaled, the results pose forth the need to impose strict regulations to CNTs in the work and habitat environment which must supersede daily regulations against asbestos.

This notion is also based on the pathological studies recently published on SWCNTs and MWCNTs [99–103]. MWCNTs were found to be genotoxic in a study on rats, where the genotoxic effect on rat lungs was observed after inhalation of MWCNTs [92]. The genotoxic effects were discussed in connection with the genotoxicity of asbestos, and their potential to lead to cancer. In context with the extrapolation to asbestos, it was observed that the genotoxicity of MWCNTs leads to clastogenic events as well as aneugenic, which both occur after DNA damage or the formation of adducts in the chromosome [100]. The induction of mutations on lung cells was thereby confirmed and well concerted with the study by Poland et al. [101] published in Nature Nanotechnology, where the asbestos-like pathology was observed. In their study the formation of granulomas, a specific type of lesion occurring when "trapped" contaminations in the organ tissues induce local clustering reactions, was observed. The formation of granulomas indicates that the nanotubes were significantly biopersistant and able to resist degradatory attempts by the immune system, known as frustrated phagocytosis [100]. SWCNTs have furthermore been shown to interfere with the duplication of cells in bronchial cell models [102]. This was observed after the association of SWCNTs with the chromosome was imaged, postulated to be occurring given CNTs resemblance to microtubulins [102]. The results showed that SWCNTs were found to be more toxic than Vanadium pentaoxide, a poisonous metal oxide. The induction of cellular damage was also documented by a group of Japanese researchers [103] who supplied data stating that MWCNTs are carcinogenic. MWCNTs were injected in rats at doses 2 mg/kg and showed development of invasive mesothelioma in various parts of the body of the rats.

5. Conclusions

The rebound effect in consumer electronics depends eventually on a vast landscape of toxicological and environmental aspects of the components used in the electricity generating units. In this review, we have discussed critically the particular environmental and adverse health effects of carbon nanotubes and fullerenes. These findings indicate that fullerenes and carbon nanotubes exert various modes of toxicological damage to bacteria, plankton, cells and multicellular organisms and are therefore exotoxic compounds. Their impacts are 3 fold due to their ability to: firstly penetrate membranes, secondly, form aggregates and thirdly, their ability to interact with different biochemical compounds. The work on fullerenes and carbon nanotubes remains unresolved and needs extensive toxicological studies and a unifying agreement and subdivision of toxicity according to their chemical mode, sizes and composition and interaction with types of organs and types of tissue in the body. This is essential work to be done before these nanoproducts become extensively incorporated in consumer electronics. In this context, consumer electronics manufacturers will use this information as a guiding light for developing environment- and health-friendly devices in the future, based on a concerted work with toxicologists and molecular biologists.

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